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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,471	06/03/2005	Larissa Balakireva	1759.200	4646

23405 7590 07/17/2007

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
07/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,471	BALAKIREVA, LARISSA	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11 and 13-15* is/are pending in the application.

4a) Of the above claim(s) *11 and 13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/3 and 7/6 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-7, 11, and 13-15 are pending in the application.

Election/Restrictions

2. Applicant's election without traverse of Group I in the reply filed on July 5, 2007 is acknowledged.

3. Claims 11, and 13-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 5, 2007.

4. Claims 1-7 are under consideration.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The information disclosure statements (IDS) submitted on June 3, and July 6, 2005, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Reference CC of the June 3, 2005 IDS has been considered to the extent of the English translation provided.

Drawings

7. The drawings are objected to because:

Figure 6A is not clear, as many of the characters appear incomplete.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

8. The disclosure is objected to because of the following informalities:

On page 1, the specification refers to the protein eIF3 without first identifying the protein by its complete name.

It is requested that the Applicant amend the specification to provide the heading "Brief Description of the Drawings" in from of the drawing summaries beginning on page 14 of the application.

It appears that reference to the HCV IRES region "Iiab" on pages 17 (line 15), 19 (lines 9, 11, and 19) should read as HCV IRES region - - IIab--.

On page 17 of the application, SEQ ID NO: 1 is identified as the "entire nucleotide sequence of the [HCV] IRES," and the entire sequence of the HCV IRES is identified as comprising positions 40-372 of the HCV genome (333 nucleotides). However, SEQ ID NO: 1 comprises only 326 nucleotides.

On page 23, the specification refers to the 16 RNA sequences selected, indicating that these are shown in Figure 6a. However, this Figure shows only 12 nucleotide sequences in addition to the sequence of the HCV IRES. Further, the sequence on line 15 is represented as corresponding to residues 56-92 of SEQ ID NO: 1. This is incorrect. The sequence appears similar to the sequence of residues 17-53 of SEQ ID NO: 1 (wherein the sequence on page 23 is missing the nucleotide corresponding to either position 54 or 55 of SEQ ID NO: 1), which in turn corresponds to residues 56-92 of domain II of the HCV IRES. Also, the sequence on line 12 fails to contain the sequence of residues 61-72 of SEQ ID NO: 1. Nor do any of the clones of Figure 6A appear to show homology to residues 84-90 of SEQ ID NO: 1.

Reference to sequences should refer to "SEQ ID NO:" or to "SEQ ID NO." instead of to "SEQ ID."

Appropriate correction is required.

9. The specification is objected to for containing referring to sequences without also identifying them by the sequence identifier assigned to them in the sequence listing as required by 37 CFR 1.821(d). See, Figures 1-2, 5B, 6A, 6B, and pages 14-15 (no SEQ ID NO has been provided for the sequences in the Figures, either in the Figures themselves or in the brief description thereof). Moreover, it is noted that the sequence identified as corresponding to SEQ ID NO: 3 on pages 5 and 13 of the application is not found in SEQ ID NO: 3. Similarly, the sequences on page 23 also do not match the indicated SEQ ID NOs (i.e. these sequences do not correspond exactly to any region of SEQ ID NO: 1, much less the identified nucleotides); reference to these sequences therefore requires the use of sequence identifiers independent of reference to SEQ ID NO: 1. Also, on page 22 (lines 12-13) it is not clear how SEQ ID NO: 14 can represent two different primers. The examiner would like to bring the applicant's attention to the following excerpt from MPEP §2422.03:

> 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. This requirement is also intended to permit references, in both the description and claims, to sequences set forth in the "Sequence Listing" by the use of assigned sequence identifiers without repeating the sequence in the text of the description or claims. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Where a sequence is embedded in the text of an application, it must be presented in a manner that complies with the requirements of the sequence rules.

The applicant is therefore required to amend the specification to comply with 37 CFR 1.821(d).

10. The disclosure is objected to because of the following informalities: it appears that reference to the HCV IRES region "Iiab" on pages 17 (line 15), 19 (lines 9, 11, and 19) should read as HCV IRES region - - IIab--.

Appropriate correction is required.

Claim Objections

11. Claim 1 is objected to because of the following informalities: the claims refers to the terms "eIF3" and "IRES" by their acronyms without first identifying them by full name. Appropriate correction is required. Moreover, eIF3 is not a protein, but is a complex of multiple proteins. See e.g., App., page 3, lines 28-30. It is therefore suggested that the claim refer to the eIF3 complex, and not refer to the complex as an individual protein.

12. Claims 2 and 3 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. These claims are not a proper dependent claim from claim 1 because it reads on material not covered by the independent claim.

Claim 1 reads on a method requiring the use of the p116 subunit. There is no disclosure in the application indicting that reference to the subunit includes portions thereof. The subunit is specifically identified as SEQ ID NO: 4, which comprises the RRM fragment of SEQ ID NO: 5. Page 7. The claim also requires the use of an HCV IRES sequence comprising at least 10 successive nucleotides of region II of SEQ ID NO: 2.

In the case of claim 2, claim 1 requires the use of the p116 subunit. However, claim 2 requires the use of only a portion of that subunit. It is therefore suggested that claim 1 be amended to read on a method of using either the p116 subunit of eIF3, or the recognition motif of this subunit.

Claim 3 requires the use of at least 8 nucleotides of SEQ ID NO: 2. Because this claim requires the use of a sequence with only 8 nucleotides from the HCV IRES sequence, whereas claim 1 requires the use of sequence of at least 10 nucleotides, claim 3 is not properly dependent on claim 1.

13. Claims 1-4, 6, and 7 are objected to because of the following informalities:

In claim 1, the steps are referred to as steps a/, b/, and c/. In claim 6, step c/ appears to be referenced as step c). Applicant should use the same terminology throughout the claims. It is suggested that claim 1 be amended to refer to steps a), b), and c). Appropriate correction is required.

In claims 1-3 and 7, the term "SEQ ID" should be replaced with - -SEQ ID NO: - -.

In claim 4, it is suggested that the claim be amended such that step b/ indicates that the absence of complex - - reflects the inhibitory capacity of the molecule tested- - or - - reflects the capacity of the molecule tested to inhibit formation of said complexes. - - The presence of both phrases is redundant and unclear.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 includes step c/, which requires that "the molecules that inhibit the formation of the complexes are selected." However, there is no antecedent basis support in the claim for "the molecules." Only a single molecule is previously identified in the claim: the molecule to be tested. It is suggested that step c/ be deleted, and step b/ be restated as two steps- one for detecting the formation of possible p116/HCV IRES complexes, and a correlation step indicating such as - - wherein an absence of p116/HCV IRES complex is reflective of the inhibitory capacity of the molecule to be tested.- -

Further, the claims are also rejected because it is not clear what HCV IRES sequences the claims are intended to read on. Claims 1 and 3 appear to read on methods wherein the HCV IRES comprises portions of one SEQ ID NOs: 2 or 3. Each of these sequences is a DNA sequence as shown by the inclusion of thymine instead of uracil in the sequences presented in the sequence listing. It is noted that the HCV IRES that associates with the eIF3 protein complex is not a DNA, but a RNA sequence. See e.g., Sizova et al., J Virol 72: 4775-82 (of record in the June 2005 IDS). This is also reflected in the language of claim 5, which reads on the detection of bound RNA. Thus, it appears that the claims should read on RNA sequences corresponding to the sequences of SEQ ID NOs: 2 or 3, and not to the sequences of SEQ ID NOs: 2 or 3 themselves. For the purposes of this action, the claims will be treated as though they referred to the RNA.

16. Claims 1, 2, and 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these claims provides reference to a composition (the p116 subunit or the HCV IRES region II) followed by a parenthetical reference to a sequence identification number. It is not clear if the reference to the sequence identifier is merely an example of the sequence that may be used, or if the claims are intended to be limited to the use of compounds with the indicated structures.

It is suggested that the claims be amended to include language such as - - the p116 subunit of SEQ ID NO: 4- - or - - the nucleotide sequence of SEQ ID NO: 2- - (the latter instead of reference to "the nucleotide sequence of region II (SEQ ID 2) of the HCV IRES").

17. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on embodiments of claim 1 wherein, respectively, "only the sequence of the recognition motif of the p116 protein (SEQ ID 5) is incubated" or "only part of region II is incubated and corresponds to the consensus sequence of SEQ ID 3 or a sequence comprising at least 8 successive nucleotides of the sequence SEQ ID 3."

These claims appear to require that either the recognition motif or the p116 protein or the indicated portion of the region II of the HCV IRES is incubated, in the absence of any of the addition materials. However, a reading of the claims as a whole suggests that the Applicant intended to require only that the method of these claims required, respectively, that only the

recognition motif of the p116 protein was incubated with the HCV IRES and the molecule to be tested, or only the part of regions II of the HCV IRES is incubated with the p116 subunit of eIF3 and the molecule to be tested.

It is suggested that claim 2 be amended to read on embodiments "wherein the p116 subunit consists of the recognition motif of the p116 protein" (in addition to the amendments suggested in the objection to claims 2 and 3 above).

It is also suggested that claim 3 be amendment to read on a method "wherein the sequence containing at least 10 nucleotides of region II of the HCV IRES is SEQ ID NO: 3, or a sequence of at least 8 successive nucleotides thereof."

For the purposes of this action, these claims will be read as though properly dependent from claim 1, wherein claim 2 excludes the presence of eIF3 sequences that the RRM sequence (represented by SEQ ID NO: 5) of the p116 protein, and claim 3 excludes HCV IRES sequences other than SEQ ID NO: 3 or fragments thereof of at least 8 nucleotides.

18. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear in this claim what it is that "corresponds to the amount of RNA bound to the membrane."

Moreover, the claim is also rejected as there is no antecedent basis support in the claims for "the mixture" referred to in line 2 of the claim, or "the radioactivity" as referred to in line 3 of the claim. . It appears that claim 5 should also include a requirement that the HCV IRES

sequence of step a/ be radioactively labeled, and that claim 1 should be amended to refer to a mixture comprising the elements of claim a/.

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to methods for screening molecules for the ability to inhibit complex formation between the HCV IRES and the eIF3 protein complex, wherein the methods involve the use of the HCV IRES sequence of SEQ ID NO: 2, the sequence of SEQ ID NO: 3, a fragment of SEQ ID NO: 2 of at least 10 nucleotides, or a fragment of SEQ ID NO: 3 of at least 8 nucleotides. Thus, these claims read on a genus of methods involving the use of any sequence of at least 10 consecutive nucleotides of SEQ ID NO: 2 or at least 8 consecutive nucleotides of SEQ ID NO: 3.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical

> and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

The present claims read on a method for screening for molecules that inhibit binding between eIF3 and the HCV IRES, particularly domain II of that protein. In order to do so, the method determines the ability of a compound to be tested to inhibit binding between eIF3 and a target HCV IRES sequence. Thus, in order for the claimed methods to be operative, there is an implicit requirement that the HCV IRES sequence used in the method be capable of binding to eIF3. The claims therefore read not only on the use of any sequence of at least 10 consecutive nucleotides of SEQ ID NO: 2 or at least 8 consecutive nucleotides of SEQ ID NO: 3, but more specifically on any such sequence that is bound by eIF3.

The teachings in the application demonstrate that HCV sequences as short as SEQ ID NO: 3 are capable of binding to eIF3. See e.g., page 23 and Figure 6A. However, the smallest region homologous to the region found in each of the sequence found to bind to eIF3 comprises 33 nucleotides. See e.g., Figure 6A, the 5_2xxx5 sequence (excluding the GAC sequence- the truncated sequence of which corresponds to the full-length sequence of SEQ ID NO: 3). The application nowhere demonstrates any smaller sequence than this that is capable of binding to the

eIF3 sequence. Thus, the disclosed species of the application are not representative of the full scope of the claimed method.

It is noted that written descriptive support does not require that species of the claimed invention be provided. However, an alternative means for identification is needed. Such may be found through the provision of a functional characteristic in combination with a structural or other non-functional identifier of the claimed compounds (or compounds used in a claimed method). In the present case, there is no non-functional identification in the application as to which 8mer(s) of SEQ ID NO: 3 or which 10mer(s) of SEQ ID NO: 2 would be capable of binding to eIF3. The application do not provide any indication as to what sequence or structure within that of SEQ ID NO: 3 is required in order for the sequence to bind eIF3. It is further noted, that, with respect to the use of any 10mer of SEQ ID NO: 2, the application also lacks support for this genus as there is no non-functional identification of any sequence that does not include SEQ ID NO: 3 which is able to bind eIF3. Because there is no non-functional identification of any sequence of at least 10 consecutive nucleotides of SEQ ID NO: 2 or at least 8 consecutive nucleotides of SEQ ID NO: 3 that are bound by eIF3, other than sequences that comprise at least SEQ ID NO: 3, the claims are rejected for having insufficient written descriptive support in the application.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 1, 4, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Sizova et al. (J Virol 72: 4775-82) and Karn et al. (WO 01/44266) (both references of record in the June 2005 IDS) and further in view of GenPept AAC99479 and in light of Pestova et al. (Genes Dev 12:67-83). These claims read on a method for screening molecules comprising incubating together a p116 subunit of the eIF3 protein complex, a nucleotide sequence of region II of the HCV IRES (or any sequence containing at least 10 consecutive nucleotides thereof), and a test compound; determining if the eIF3 protein forms a complex with the HCV RNA, and thereby identifying compounds that inhibit eIF3/HCV IRES complex formation. Claims 6 and 7 are drawn to method as described above, wherein after potential inhibitors have been identified, the compounds are then tested ex vivo for the ability to inhibit cap-dependent viral replication through the use of bicistronic vector consisting of two luciferase vectors framing a sequence comprising SEQ ID NO: 2, 3, or any sequence containing at least 10 nucleotides thereof.

Sizova teaches that the HCV IRES binds to the eIF3 protein p116. See e.g., abstract. The reference also teaches a method which resulted in a direct detection of binding between these two compounds. See e.g., page 4779 (section spanning the two columns). However, the reference does not teach or suggest the use of such a method for the detection of inhibitors of such bindings.

Karn teaches that inhibitors of HCV IRES binding by eIF3 are a source of potential HCV therapeutics. Page 1, lines 8-9. Karn also indicates that indirect methods of measuring the inhibition of such binding have certain drawbacks, and therefore suggests the use of direct

measurements of IRES/protein binding for the identification of inhibitors thereof. Page 1, lines 21-27. From these teachings, and in view of the demonstration of a method showing direct binding between these compounds in Sizova, it would have been obvious to those of ordinary skill in the art to use the binding assay of Sizova as a means for the identification of binding inhibitors by performing the assay in the presence of test compounds. Moreover, it would have been obvious to those of ordinary skill in the art to have performed multiple such tests in the presence and absence of the test compounds, and thus with increasing dosages of the compound. It is noted that the present claims do not exclude the presence of additional sequences from that of SEQ ID NO: 2 in the HCV IRES sequence used in the claimed method.

It is noted that the Sizova reference does not disclose the entire sequence of the HCV IRES used therein. However, the reference indicates that the sequence used was that used in the Pestova reference. See, page 4776 (section titled "Plasmids"). Pestova discloses an HCV IRES sequence including at least 10 residues of SEQ ID NO: 2. See, page 69, Figure 1A. Thus, the limitation that the HCV IRES comprises a sequence having at least 10 nucleotides of SEQ ID NO: 2 is met. Nor does the Sizova reference teach the sequence of the eIF3, or of p116 in specific. Nonetheless, as shown by GenPept AAC99479, SEQ ID NO: 4 was a recognized sequence of p116 (also referred to as the p110 subunit). Thus, it would have been obvious to those of ordinary skill in the art to have used the p116 of SEQ ID NO: 4 in the method suggested by Sizova and Karn. This is because it would have been recognized that the p116 of the indicated accession was a functional equivalent for isolated p116.

In addition to the teachings described above, it is noted that the Karn reference also refers to an indirect method for the identification of RNA/protein binding inhibitors comprising the use

of a construct such as that described in claim 5. Page 1, lines 10-20. The reference indicates that such a construct is useful for determining the ability of a compound to inhibit translation of proteins under the control of the viral IRES. Id. Because the reference indicates that such constructs are useful for measuring the ability of a compound to actually inhibit viral RNA mediated translation, it would have been obvious to those of ordinary skill in the art to have used such methods in combination with the direct identification methods so as to confirm the ability of an identified compound to actually inhibit translation of the HCV genome. It would therefore have been obvious to those of ordinary skill in the art to have made such a construct including the HCV IRES and to have used such to measure the ability of a compound identified by the method of claim 1 to actually inhibit HCV translation.

The combined teachings of these references therefore render the claimed methods obvious.

23. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sizova, Karn, Pestova, and GenPept AAC99479 as applied to claims 1 and 4 above, and further in view of Mei et al. (Bioorganic & Medical Chemistry, 5:1173-1184). This clam limits the method of claim 1 to embodiments wherein the detection of the p116/IRES complex is carried out by filtering the incubated mixture of HCV IRES RNA, eIF3/p116, and the test compound through a nitrocellulose membrane, and detecting the presence of the RNA on the membrane through use of a radioactive label. The teachings of the previously applied references have been described above. These references do not specifically teach the method of claim 5.

However, such a method for the identification of inhibitors of protein/RNA binding would have been obvious based on the teachings of the previously applied references, teaching the incubation and formation of a complex among the compounds of claim 1, and the teachings of Mei, which indicates that methods such as that described in claim 5 were known in the art. See, Mei, pages 1176 (describing the filtration assay) and 1179 (left column- teaching the use of filtration assays to identify protein/RNA binding inhibitors). Because Mei teaches that such an assay is effective for the identification of inhibitors of protein/RNA binding, and as the previously described teachings suggest the identification of inhibitors of HCV IRES binding to eIF3/p116, it would have been obvious to those of ordinary skill in the art to have used such an assay for the identification of such HCV inhibitors. The combined teachings of these references therefore render the claimed inventions obvious.

Conclusion

24. No claims are allowed.

25. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Collier et al., J Gen Virol 79: 2359-66. This reference provides further teachings on the use of constructs such as described by claim 7. The reference is therefore considered to support, and redundant to, the teachings of Karn with respect to claims 6 and 7.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Z. Lucas/
Patent Examiner, AU 1648